Title: USE OF METABOLIC PHENOTYPING....

Inventor: Brian Leyland-Jones

Basic Structure of N-(Aryl Substituted) - naphthalidimides

Title: USE OF METABOLIC PHENOTYPING....

Inventor: Brian Leyland-Jones

NAT2

1X (1-methylxanthine)

$$H_3C$$
 NH
 CH_3
 NH_2

AAMU (5-acetamino-6-amino-methyluracil)

AFMU (5-acetamino-6-formylamino-methyluracil)

Fig. 2

Title: USE OF METABOLIC PHENOTYPING....

Inventor: Brian Leyland-Jones

CYP1A2

Caffeine (1,3,7-trimethylxanthine)

1,7-DMX (1,7-dimethylxanthine)

1,7-DMU (1,7-dimethyluracil)

Fig. 3

Title: USE OF METABOLIC PHENOTYPING....

Inventor: Brian Leyland-Jones

CYP3A4

MDZ (Midazolam)

1-OH-MDZ (1-Hydroxymidazolam)

Title: USE OF METABOLIC PHENOTYPING....

Inventor: Brian Leyland-Jones

NAT1

p-ASA (p-aminosalicylic acid)

Acetyl-pASA (acetyl-p-aminosalicylic acid)

Title: USE OF METABOLIC PHENOTYPING....

Inventor: Brian Leyland-Jones

CYP2A6

Coumarin

7-Hydroxycoumarin

Title: USE OF METABOLIC PHENOTYPING....

Inventor: Brian Leyland-Jones

CYP2C19

R-(-)-Mephenytoin

S-(+)-Mephenytoin

Title: USE OF METABOLIC PHENOTYPING....

Inventor: Brian Leyland-Jones

CYP2C9

(s)-Ibuprofen

2-carboxvibuprofen

Title: USE OF METABOLIC PHENOTYPING....

Inventor: Brian Leyland-Jones

CYP2D6

Dextromethorphan

Dextrorphan

Title: USE OF METABOLIC PHENOTYPING....

Inventor: Brian Leyland-Jones

CYP2E1

Clorzoxazone

6-Hydroxychlorzoazone

Title: USE OF METABOLIC PHENOTYPING....

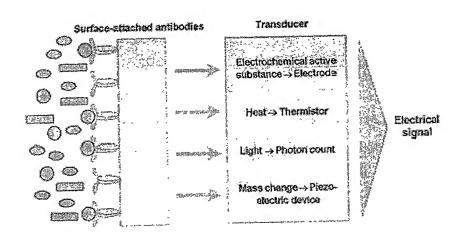


Fig. 11

Title: USE OF METABOLIC PHENOTYPING....

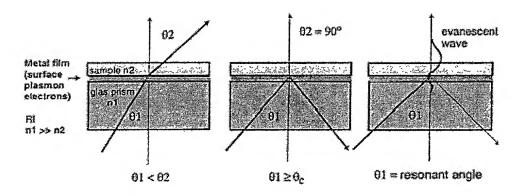


Fig. 12

Title: USE OF METABOLIC PHENOTYPING....

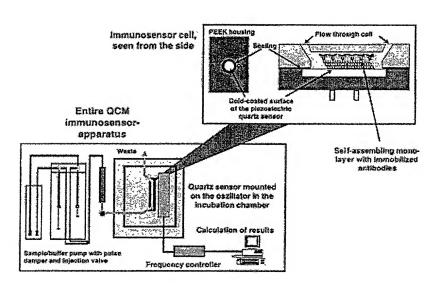


Fig. 13

AAMU-hemisuccinic acid

1 methyl xanthine-8-propionic acid

Fig. 14

Derivatives of AAMU (5-acetamino-6-amino-3-methyluracil) or AFMU (5-acetamino-6-formylamino-3-methyluracil)

Where Y

X

 (CH_2) n-COOH

where n = 2,3 or 4

$$(CH_2)$$
 $n-C-NH-NH_2$

$$(CH_2) n - C - NH - (CH_2) n - NH_2$$

 $CH_2 - X'$

where X' is I, Br, or Cl

$$CH_2-S-(CH_2)n-NH_2$$

Derivatives of AAMU (5-acetamino-6-amino-3-methyluracil) or AFMU (5-acetamino-6-formylamino-3-methyluracil)

$$\begin{array}{c} H \\ O \\ N \\ - C \\ C \\ C \\ O \\ O \\ \end{array}$$

Where Y is

Х

$$(CH_2)n-COOH$$

where n = 2,3 or 4

$$(CH_2)n-C-NH-NH_2$$

$$CH_2-X$$

where X' is I, Br, or Cl

$$CH_2-S-(CH_2)n-NH_2$$

$$\mathrm{CH_2}\mathrm{-s-CH_2}\mathrm{-cH_2}\mathrm{-oH}$$

Derivatives of 1X (methylxanthine)

$$CH^3$$
 N
 N
 N
 X

X

$$(CH_2)n-COOH$$

where n = 2,3 or 4

$$(CH_2)n-C-NH-NH_2$$

$$(CH_2) n - C - NH - (CH_2) n - NH_2$$

$$(CH_2) n - C - NH - (CH_2) n - SH$$

Derivatives of 1X (methylxanthine)

X

$$(CH_2)$$
 $n-COOH$

where n = 2,3 or 4

$$(CH_2) n - C - NH - (CH_2) n - NH_2$$

$$(CH_2) n - C - NH - (CH_2) n - SH$$

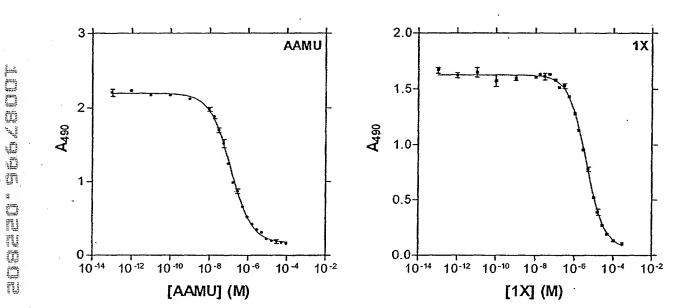
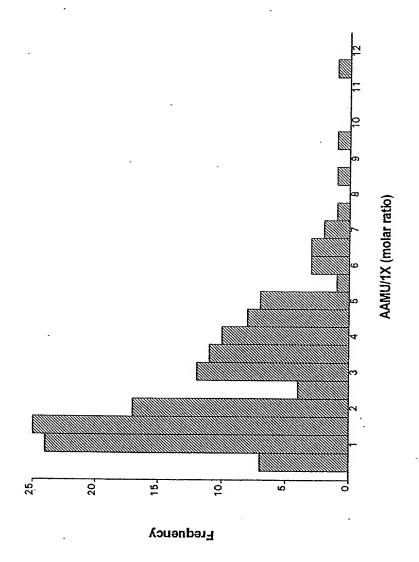


Fig. 19



Docket No.: 3298.1003-000 Title: USE OF METABOLIC PHENOTYPING....

CH3 Br(CH₂)₅COOCH₂CH₃ CH2(CH2)4COOCH2CH3 СНз CH₃ II NaOH ÇH₂(СН₂)₄СООН CH₃ ĊНз

Caffeine derivative

 CH_3 IV $Br(CH_2)_5COOCH_2CH_3$ сн₂(сн₂)₄соосн₂сн₃ CH3 NH NaOH ÇH2(CH2)4СООН CH₃ ۷ſ

1,7-dimethylxanthine derivative

Fig. 21

$$\begin{array}{c} O & (CH_2)_4NHBOC \\ CH_3 & N & COOCH_2CH_3 \\ O & N & NH_2 & O & N & N \\ XV & XVI & XVI & XVI \end{array}$$

1,7-dimethyluric acid derivative

Fig. 22

12	STD16	STD17	STD18	STD19	STD20	STD21	STD22	STD23	
T T	STD8	STD9	STD10	STD11	STD12	STD13	STD14	STD15	
10	Blk	STD1	STD2	STD3	STD4	SIDS	STD6	STD7	
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. 63	STD8	STD9	STD10	STD11	STD12	STD13	STD14	STD15	
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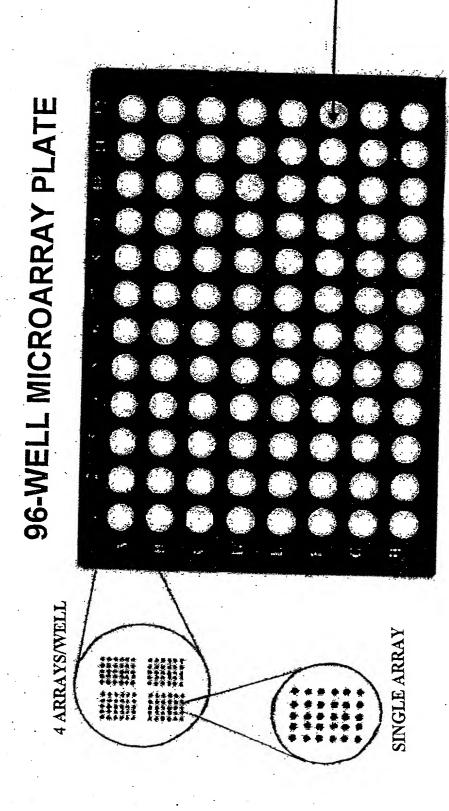
Litle: USE OF METABOLIC PHENOTYPING....

Fig.

ANTIGEN KEY:	1. BIOTINYLATED BSA MARKER 2-6. BUFFER BLANKS 7. NAT2: AAMU	8. BIOTINYLATED BSA MARKER 9. NAT2: 1X 10. NAT1: pASA	2: C: C:	7	16. CYP2A6: COMARIN 71. CYP2A6: 7-HYDROXYCOUMARIN		19. BIOTINYLATED BSA MARKER 20. CYP2C19: S-(+)-MEPHENYTOIN	. CYP2C9:	22. CYP2C9: 4-HYDROXYDICLOFENAC 23. CYP2D6: DEXTROMETHORPHAN	24. CYP2D6: DEXTRORPHAN		27. CYP2E1: 6-HYDROXYCHLORZOXAZONE	CYP3A4:	i	31-36. BIOTINYLATED BSA MARKER
	g	(E)	(¥)	(H)	(g	-)							
	•	•	•	•)	(2))	UT:						
6 ARRAY	•	•		•			(E)	ARRAY LAYOUT:	(RS-C		. xs.	•	-SN:
	•	•	•	•	•		ū)	RAY	-	T MARKERS -	i i	BUFFER BLANKS .		ANTIGENS -
y 9	•		•	•	•		E)	AR		ALIGNMENT		BLFF		
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Title: USE OF METABOLIC PHENOTYPING....



Inventor: Brian Leyland-Jones Title: USE OF METABOLIC PHENOTYPING....

Title: USE OF METABOLIC PHENOTYPING....

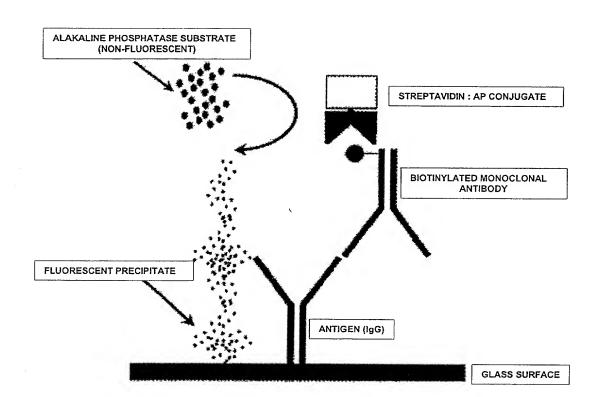


Fig. 26

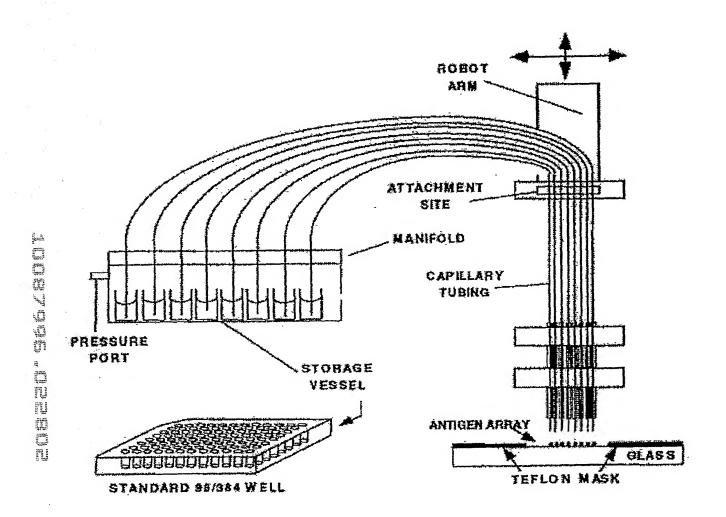
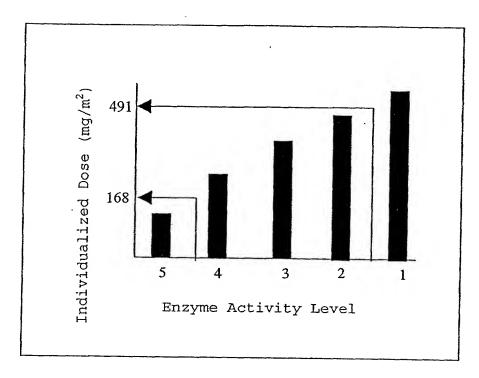


Fig. 27

Title: USE OF METABOLIC PHENOTYPING....



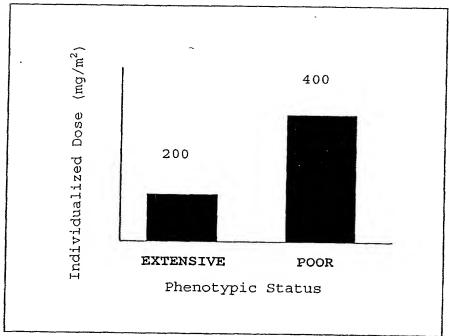


Fig. 28

195

190

185

- 180 175

- 170

155

-120 H H H H H H H H H

105

-100

Docket No.: 3298.1003-000

Title: USE OF METABOLIC PHENOTYPING....

Inventor: Brian Leyland-Jones

Nomogram for the Determination of Body Surface Area (BSA)

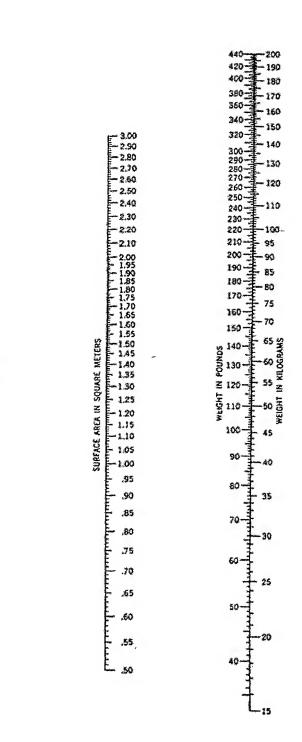


Fig. 29